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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Muthiah Manoharan

Serial No.: 09/965,551

Group Art Unit: Not Yet Assigned

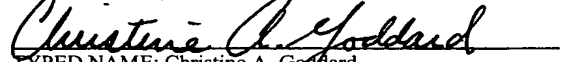
Filing Date: September 27, 2001

Examiner: Not Yet Assigned

For: CARBOHYDRATE OR 2'-MODIFIED OLIGONUCLEOTIDES HAVING
ALTERNATING INTERNUCLEOSIDE LINKAGES

DATE OF DEPOSIT: November 5, 2001

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TYPED NAME: Christine A. Goddard
REGISTRATION NO: 46,731

Assistant Commissioner for Patents
Washington DC 20231

Dear Sir:

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §1.56 and in accordance with 37 C.F.R. §§1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 C.F.R. §1.56(b).



In accordance with §1.97(b), since this Information Disclosure Statement is being

filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of the above identified application as set forth in §1.491, before the mailing date of a first Office Action on the merits of the above-identified application, or before the mailing date of a first office action after the filing of request for continued examination under §1.114, no additional fee is required.

- ☐ In accordance with §1.129(a), this Information Disclosure Statement is being filed in connection with ☐the first or ☐second After Final Submission, therefore:
- ☐ Certification in Accordance with §1.97(e) is attached; or
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- ☐ Copies of each of the references listed on the attached Form PTO-1449 are enclosed herewith.
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- EXCEPT THAT:
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☒ In accordance with §1.98(d), copies of the following references listed on the attached Form PTO-1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C. §120 have been made in the instant application:

☒ Copies of references **AA-CO, CQ-DP, DR, DS, DU-DX, DZ-ES**, listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior application Serial No. **09/349,007**, filed **July 7, 1999**.

☐ If any of the foregoing publications are not available to the Examiner, Applicant will endeavor to supply copies at the Examiner's request.


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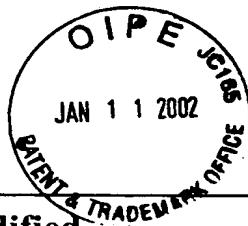

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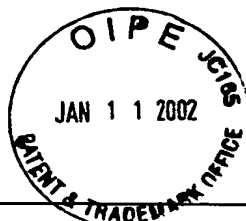


Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-4847	Serial No. 09/965,551
		Applicant Muthiah Manoharan	
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	AA	Albert, P.R. et al., "Antisense knockouts: molecular scalpels for the dissection of signal transduction", <i>Trends Pharmacol. Sci.</i> , 1994 , <i>15</i> , 250-254	
*	AB	Ausubel, F.M. et al., (eds.), <i>Current Protocols in Molecular Biology</i> , Current Publications, 1993	
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	AH	Bernhard et al., "Direct Evidence Linking Expression of Matrix Metalloproteinase 9 (92-kDa gelatinase/collagenase) to the metastatic phenotype in transformed rat embryo cells," <i>Proc. Natl. Acad. Sci. U.S.A.</i> , 1994 , <i>91</i> , 4293-4297	
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	AK	Cook, P.D., "Medicinal chemistry of antisense oligonucleotides - future opportunities", <i>Anti-Cancer Drug Design</i> , 1991 , <i>6</i> , 585-607	
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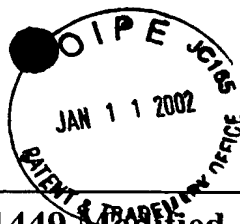
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	AR	Griffiths, C.E.M. et al., "Keratinocyte Intercellular Adhesion Molecule-1 (ICAM-1) Expression Precedes Derman T Lymphocyte Infiltration in Allergic Contact Dermatitis (<i>Rhus dermatitis</i>)", <i>Am. J. Pathology.</i> , 1989 , 135, 1045-1053	
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	AW	Ho, V.C. et al., "Treatment of severe lichen planus with cyclosporine", <i>J. Am. Acad. Dermatol.</i> , 1990 , 22, 64-68	
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	BA	Katocs, A.S. et al., "Biological Testing", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, 1990 , Ch. 27, 484-494	
	BB	Kerr et al., "TGF-B1 Inhibition of Transin/Stromelysin Gene Expression Is Mediated Through a Fos Binding Sequence," <i>Cell</i> , 1990 , 61, 267-278	
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	BF	Lisby, S. et al., "Intercellular adhesion molecule-1 (ICAM-1) expression correlated to inflammation", <i>Br. J. Dermatol.</i> , 1989 , 120, 479-484	
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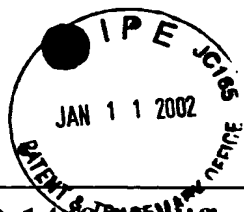
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	BH	Manoharan, M. et al., "Introduction of a Lipophilic Thioether Tether in the Minor Groove of Nucleic Acids for Antisense Applications", <i>Bioorg. Med. Chem. Letts.</i> , 1993 , 3, 2765-2770	
	BI	Manoharan, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides", <i>Annals NY Acad. Sciences</i> , 1992 , 660, 306-309	
*	BJ	Manoharan, M., <i>Antisense Research and Applications</i> , Crooke et al. (eds.), CRC Press, Boca Raton, 1993	
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	BL	Manoharan, M. et al., "Lipidic Nucleic Acids", <i>Tetrahedron Letts.</i> , 1995 , 36, 3651-3654	
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	BP	Mishra, R.K. et al., "Improved leishmanicidal effect of phosphorothioate antisense oligonucleotides by LDL-medicated delivery", <i>Biochim. Et Biophysica</i> , 1995 , 1264, 229-237	
	BQ	Newman, "The Biology of PECAM-1," <i>J. Clin. Invest.</i> , 1997 , 99, 3-7	
	BR	Nies, A.S. et al., "Principles of Therapeutics", <i>Goodman & Gilman's The Pharmacological Basis of Therapeutics</i> , 9th Ed., Hardman et al. (eds.), McGraw-Hill, New York, NY, 1996 , Ch. 3, 43-62	
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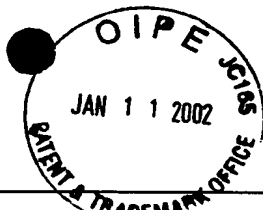


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	BT	Regezi et al., "Vascular Adhesion Molecules in Oral Lichen Planus," <i>Oral Surg. Oral Med. Oral Pathol.</i> , 1996 , <i>81</i> , 682-690	
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	BZ	Shea, R.G. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucleotide conjugates", <i>Nucl. Acids Res.</i> , 1990 , <i>18</i> , 3777-3783	
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	CB	Smith-Jones, P.M. et al., "Antibody Labeling with Copper-67 Using the Bifunctional Macrocycle 4-[(1,4,8,11-Tetraazacyclotetradec-1-yl)methyl] benzoic Acid", <i>Bioconjugate Chem.</i> , 1991 , <i>2</i> , 415-421	
	CC	Stetler-Stevenson et al., "Tumor Cell Interactions with the Extracellular Matrix During Invasion and Metastasis," <i>Annu. Rev. Cell Biol.</i> , Palade, G.E. et al. (eds.), 1993 , <i>9</i> , 541-573	
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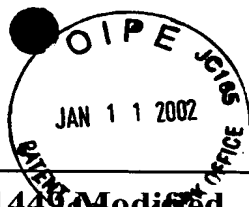
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	CD	Studer, M. et al., "One-Step Synthesis of Mono-N-substituted Azamacrocycles with a Carboxylic Group in the Side-Chain and their complexes with Cu ²⁺ and Ni ²⁺ ", <i>Helvetica Chimica Acta</i> , 1986 , 69, 2081-2086	
	CE	Svinarchuk, F.P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups", <i>Biochimie</i> , 1993 , 79, 49-54	
	CF	U.S. Congress, Office of Technology Assessment, "The State-of-the-art in Genetic Screening", <i>Genetic Monitoring and Screening in the Workplace</i> , OTA-BA-455, U.S. Government Printing Office, Washington, D.C., 1990 , Ch. 5, 77-99	
	CG	Wahlestedt, C. et al., "Modulation of Anxiety and Neuropeptide Y-Y1 Receptors by Antisense Oligodeoxynucleotides", <i>Science</i> , 1993 , 259, 528-531	
	CH	Wahlestedt, C. et al., "Antisense oligodeoxynucleotides to NMDA-R1 receptor channel protect cortical neurons from excitotoxicity and reduce focal ischaemic infarctions", <i>Nature</i> , 1993 , 363, 260-263	
	CI	Zhang, Z. et al., "Uptake of N-(4'-pyridoxyl)amines and release of amines by renal cells: A model for transporter-enhanced delivery of bioactive compounds", <i>Proc. Natl. Acad. Sci.</i> , 1991 , 88, 10407-10410	
	CJ	Delgado, C. et al., "The Uses and Properties of PEG-Linked Proteins", <i>Crit. Rev. in Therapeutic Drug Carrier Sys.</i> , 1992 , 9, 249-304	
	CK	Hamm, M. L. et al., "Incorporation of 2'-Deoxy-2'-mercaptocytidine into Oligonucleotides via Phosphoramidite Chemistry," <i>J. Org. Chem.</i> , 1997 , 62, 3415-3420	
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	CO	Thomson, J. B. et al., "Synthesis and Properties of Diuridine Phosphate Analogues Containing Thio and Amino Modifications," <i>J. Org. Chem.</i> , 1996 , 61, 6273-6281	
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	CP	Akhtar et al., "Stability of antisense DNA oligodeoxynucleotide analogs in cellular extracts and sera", <i>Life Sciences</i> , 1991 , 49, 1793-1801	
	CQ	"Antisense '97: A roundtable on the state of the industry," <i>Nature Biotech.</i> , June 1997 , 15, 519-524	
	CR	Cucco, C. et al., "In Vitro and in Vivo Reversal of Multidrug Resistance in a Human Leukemia resistant Cell Line by <i>mdr1</i> Antisense Oligodeoxynucleotides," <i>Canc. Res.</i> , 1990 , 4332-4337	
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	CT	Furdon, P. J. et al., "RNase H Cleavage of RNA hybridized to oligonucleotides containing methylphosphonate, phosphorothioate and phosphodiester bonds," <i>Nucl. Acids Res.</i> , 1989 , 17, 9193-9204	
	CU	Gerwitz, A. M. et al., "Facilitating oligonucleotide delivery: Helping antisense deliver on its promise," <i>Proc. Natl. Acad. Sci.</i> , 1996 , 93, 3161-3163	
	CV	Gura, T., "Antisense has Growing Pains," <i>Science</i> , 1995 , 270, 575-577	
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	DA	Monia, B. P. et al., "Antitumor activity of a phosphorothioate antisense oligodeoxynucleotide targeted against C-raf kinase," <i>Nature Med.</i> , 1996 , 2(6), 668-675	
	DB	Neurath, M. F. et al., "Local administration of antisense phosphorothioate oligonucleotides to the p65 subunit of NF-kB abrogates established experimental colitis in mice," <i>Nature Medicine</i> , 1996 , 2(9), 998-1004	
	DC	Offensperger, W. B. et al., "Antisense Therapy of Hepatitis B Virus Infection," <i>Methods in Molecular Medicine: Antisense Therapeutics</i> , date unlisted, Agarwal, S., ed., 143-158	
	DD	Offensperger et al., "In vivo inhibition of duck hepatitis B virus replication and gene expression by phosphorothioate modified antisense oligodeoxynucleotides", <i>The EMBO Journal</i> , 1993 , 12(3), 1257-1262	
	DE	Oberbauer et al., "In vivo suppression of the renal Na ⁺ /P _i cotransporter by antisense oligonucleotides", <i>PNAS:Physiology</i> , May 1996 , 93, 4903-4906	
	DF	Patil, S. V. et al., "Syntheses and Properties of Oligothymidylate Analogs Containing Stereoregulated Phosphorothioate and Phosphodiester Linkages in an Alternating Manner," <i>Bioorganic & Medicinal Chem. Letts.</i> , 1994 , 4(22), 2663-2666	
	DG	Rojanasakul, Y., "Antisense oligonucleotide therapeutics: drug delivery and targeting," <i>Advanced Drug Delivery Reviews</i> , 1996 , 18, 115-131	
	DH	Simons, M. et al., "Antisense c-myb oligonucleotides inhibit intimal arterial smooth muscle cell accumulation in vivo," <i>Nature</i> , 1992 , 359, 67-70	
	DI	Stull, R. A. et al., "Antigene, Ribozyme and Aptamer Nucleic Acid Drugs: Progress and Prospects," <i>Pharmac. Res</i> , 1995 , 12, 465-483	
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				Applicant Muthiah Manoharan			
				Filing Date September 27, 2001		Group Not Yet Assigned	
U. S. PATENT DOCUMENTS							
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	DJ	3,687,808	08/29/72	Merigan et al.	195	28	
	DK	4,689,320	08/25/87	Kaji	514	44	
	DL	4,806,463	02/21/89	Goodchild et al.	435	5	
	DM	5,004,810	04/02/91	Draper	536	27	
	DN	5,166,195	11/24/92	Ecker	514	44	
	DO	5,194,428	03/16/93	Agrawal et al.	514	44	
	DP	5,212,295	05/18/93	Cook	536	26.7	
	DQ	5,220,007	06/15/93	Pederson et al.	536	23.1	
	DR	5,242,906	09/07/93	Pagano et al.	514	44	
	DS	5,248,670	09/28/93	Draper et al.	514	44	
	DT	5,264,423	11/23/93	Cohen et al.	514	44	
	DU	5,442,049	08/15/95	Anderson et al.	536	24.5	
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Examiner Initial		Document No.	Date	Country	Translation YES NO		
	DV	WO 93/07883	04/29/93	PCT	X		
	DW	WO 93/18052	09/16/93	PCT	X		
	DX	WO 94/08003	04/14/94	PCT	X		
	DY	WO 95/13834	05/26/95	PCT	X		
EXAMINER				DATE CONSIDERED			



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	DZ	5,457,189	10/10/95	Crooke et al.	536	24.5
	EA	5,514,577	05/07/96	Draper et al.	435	238
	EB	5,514,788	05/07/96	Bennett et al.	536	23.1
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	ED	5,580,767	12/03/96	Cowsert et al.	435	172.3
	EE	5,582,972	12/10/96	Lima et al.	435	6
	EF	5,582,986	12/10/96	Monia et al.	435	6
	EG	5,587,361	12/24/96	Cook et al.	514	44
	EH	5,591,600	01/07/97	Ecker	435	69.1
	EI	5,591,623	01/07/97	Bennett et al.	435	240.2
	EJ	5,591,720	01/07/97	Anderson et al.	514	44
	EK	5,599,797	02/04/97	Cook et al.	514	44
	EL	5,607,923	03/04/97	Cook et al.	514	44
	EM	5,620,963	04/15/97	Cook et al.	514	44

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Examiner Initial		Document No.	Date	Country	Translation YES NO	

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	EN	5,658,891	08/19/97	Draper et al.	514	44
	EO	5,661,134	08/26/97	Cook et al.	514	44
	EP	5,681,747	10/28/97	Boggs et al.	435	375
	EQ	5,681,944	10/28/97	Crooke et al.	536	24.5
	ER	5,691,461	11/25/97	Ecker et al.	536	24.32
	ES	5,670,633	09/23/97	Cook et al.	536	23.1
	ET	5,877,309	03/02/99	Dean et al.	536	24.5
	EU	5,955,443	09/21/99	Bennett et al.	514	44
	EV	5,985,558	11/16/99	Dean et al.	435	6
	EW	6,111,094	08/29/00	Bennett et al.	536	024
	EX	6,127,533	10/03/00	Cook et al.	536	23.1
	EY	6,166,197	12/26/00	Cook et al.	536	024
	EZ	6,172,209	01/09/01	Manoharan et al.	536	023
	FA	6,271,358	08/07/01	Manoharan et al.	536	023
	FB	6,277,967	08/21/01	Manoharan	536	22.1
	FC	6,300,491	10/09/01	Bennett et al.	536	024

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					YES	NO

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